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PRE-APPEAL BRIEF REQUEST FOR REVIEW	Docket Number (Optional) 55682CON(71432)

Application Number	Filed
10/758,233-Conf. #5334	January 13, 2004

First Named Inventor: Poul E. Bertelsen et al.

Art Unit	Examiner
1615	A. Sasan

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- [ ] applicant /inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [x] attorney or agent of record. Registration number 51,615
- [ ] attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34. _____

/Nicholas J. DiCeglie, Jr./
Signature

Nicholas J. DiCeglie, Jr.
Typed or printed name

(212) 308-4411
Telephone number

November 16, 2010
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

- [ ] *Total of 1 forms are submitted.

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4).

Dated: November 16, 2010 Electronic Signature for Nicholas J. DiCeglie, Jr.: /Nicholas J. DiCeglie, Jr./

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Dated: November 16, 2010
Electronic Signature for Nicholas J. DiCeglie, Jr.: /Nicholas J. DiCeglie, Jr./

Docket No.: 55682CON(71432)
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Poul E. Bertelsen

Application No.: 10/758,233 Confirmation No.: 5334

Filed: January 13, 2004 Art Unit: 1615

For: QUICK RELEASE PHARMACEUTICAL COMPOSITIONS OF DRUG SUBSTANCES Examiner: A. Sasan

REMARKS/ARGUMENT IN SUPPORT OF
PRE-APPEAL BRIEF REQUEST FOR REVIEW

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

The following remarks support Applicant's "Pre-Appeal Brief Request for Review" filed herewith in the above-referenced application. These remarks constitute no more than five pages, and are being filed with a Notice of Appeal, thereby satisfying the requirements.

Claims 68, 70-72, 75-80, 82, 83, 85-86, 91-92, 95-96, 108, 109, 111 and 119-126 are rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Nemoto et al. (JP 03-240729) in view of Klioze et al. (US 2,887,439).

Claims 87-90, 93-94 and 115-118 are rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Nemoto et al. (JP 03-240729) in view of Klioze et al. (US 2,887,439) and Penkler et al. (US 5,854,226).

Applicant respectfully requests review of the Final Office Action in the above-referenced application. No amendments are being filed with this request. Applicant is filing the "Pre-Appeal Brief Request for Review" based on the following clear errors and/or omissions in the Final Office Action mailed on June 17, 2010.[1] As both the rejections rely on the improper

[1] As an initial comment, Applicant notes that the Examiner has not considered Japanese Patent Documents JP 5-112445 and JP 5-271054 as they were "not in English". Applicant respectfully notes that US 5,424,075 and EP 0

combination of Nemoto and Klioze only that combination of references will be discussed in detail. Penkler does not overcome the deficiencies of the combination of Nemoto and Klioze.

First Clear Error and/or Omission in the Final Office Action:

The Examiner has made a first clear error and/or omission at least because the instantly claimed invention is not obvious in view of the cited art as no reasoned explanation of a motivation to combine the references is provided.

The Office Action states:

> One of ordinary skill in the art would do this because Klioze teaches that granules… [of] (149µM to 840µM) are most advantageous in preparing palatable, rapidly disintegrable tablets comprising compressed granules…. One of ordinary skill in the art would have a reasonable expectation of success…. (page 5)
>
> ***
>
> Klioze discloses granules that are between 149µm to 840µm, which are used for rapidly disintegrable and rapidly dissolvable tablets, thereby providing motivation for one of ordinary skill in the art to use granules in this size range for tablets designed for rapid disintegration and/or rapid dissolution. (Page 13)

Nemoto prepares granules using a 20-mesh screen (page 5) which is within the teachings of Klioze. As Klioze teaches no preference for smaller granules, there can be no motivation to modify Nemoto within the teachings of Klioze as there is no expected advantage. A proper rejection must provide a reasoned explanation of why one of skill in the art when already within the teachings of Klioze would select the specifically asserted value within Klioze with no expected advantage. Those of skill in the art would understand that granule size is selected based on final tablet size, not for modifying dissolution properties.[2]

In *Crocs, Inc. v U.S. International Trade Commission* (citation omitted, discussed in the Guidelines), the claimed components were a one piece molded foam base clog and a strap also made of foam to support the wearer's foot. A first reference taught a foam base clog and a second reference taught a strap of elastic or other stretchable material. "The prior art depicts foam as unsuitable for straps." Each component was well known in the art. The Guidelines say that the case "serves as a reminder to Office personnel that merely pointing to the presence of all of the claim elements in the art is not a complete statement of a rejection for obviousness." For this reason, the rejection set forth is improper.

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553 777, which were considered by the Examiner, are the English Language equivalents of the Japanese Patent Documents, respectively. Reconsideration is respectfully requested.

[2] *Remington's*, 16th Edition, p. 1563 and *Remington*, 21st Edition, p. 898

Nemoto provides a method to adjust the dissolution rate by varying the amount of various tablet components.[3] No reference has been provided by the Office to demonstrate that decreasing granule size to the size claimed would increase dissolution rate.[4] The references of record teach that a decrease in granule size, if anything, decreases dissolution rate.[5] Further, the references of record teach that decreasing granule size increases difficulties in tableting.[6] The Office Action merely points to elements in the cited art, i.e., granule size and tablet components, and provides no motivation to combine the references.

Second Clear Error and/or Omission in the Final Office Action:

The Examiner has made a second clear error and/or omission at least because the instantly claimed invention is not obvious in view of the cited art as the art teaches against the modification of Nemoto to use granules of the size instantly claimed.

Klioze teaches granules as small as 149μM can be used in tablet preparation. However, Klioze also teaches the removal of all granules smaller than 149 μM (col. 4, ln 34-35) and that the presence of excess small granules causes difficulties in tableting (col 2, ln 49-53).[7] The prior art as a whole teaches small granules as being unsuitable for tablet preparation. Nemoto is concerned with the preparation of a formulation suitable for tableting.[8]

Further, the Office Action states that "one of ordinary skill in the art at the time of the invention was made would have found it obvious to look at **all pertinent art**, including… Klioze ". (Page 13, emphasis in original) The rejection fails to consider Klioze as a whole or **all pertinent art**. Klioze **as a whole** cautions against the use of excess small granules.[5] When

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[3] "Thus there would have been no motivation to modify the initial formulation, even though the modification could have been done. Moreover a person of skill in the art would have chosen a different modification even if he or she had recognized the problem" Guidelines, page 53646, third col., discussing *In re Omeprazole Patent Litigation* regarding inclusion of a second coating on omeprazole tablets.

[4] "If optimization of the application parameters had not been within the level of ordinary skill in the art, the outcome of the *Ecolab* case may well have been different." "Examinations Guidelines Update: Development in the Obviousness Inquiry after *KSR v. Teleflex*" published in the *Federal Register* on September 1, 2010 (hereinafter Guidelines), page 35648, col. 2, discussing that the optimization of pressure in the Ecolab case was admitted to be a results effective variable, but that if it had not been, that the modification of a non-results effective variable might not have been obvious.

[5] See, e.g., Faith submitted with Response to Office Action on September 28, 2009

[6] "Even though the components are known, the combining step is technically feasible, and the result is predictable, the claimed invention may nevertheless be non-obvious when the combining step involves such additional effort that no one of ordinary skill would have undertaken it without recognized reason to do so." Guidelines, page 53646, col. 2; Lieberman, vol. 1, p. 148, vol. 2, pp. 33-34.

[7] Pages 11-12 of Office Action response of 11/23/2009

[8] Pages 12-13 of Office Action response of 11/23/2009

looking at **all pertinent art**, one would consider the references of record[9] to confirm cautionary statements made in Klioze[10] regarding the use of excess small granules. The art teaches repeatedly that small granules (e.g., less than 100-mesh, i.e., 149μM per Klioze) should be removed prior to tableting to allow for efficient tableting and tablets that do not split (*Remington's Pharmaceutical Sciences,* 16th Edition) to provide granules with good fluidity (e.g., 200-250 μM per Lieberman) to permit tableting.[11] The Guidelines state:

> An inference that a claimed combination would not have been obvious is especially strong where the prior art's teachings undermine the very reason being proffered as to why a person of ordinary skill would have combined the known elements.[12]

The combination of references suggested in the Office Action undermine the very reason being proffered as to why a person of ordinary skill would have combined the known elements as the combination would result in a material less suitable for preparation of a tablet.

> A claimed combination of prior art elements may be nonobvious where the prior art teaches away from the combination and the combination yields more than predictable results.[13]

The decreased granule size claimed provides more than predictable result, e.g., better dissolution rate, without the disadvantages taught by the prior art, e.g., poor tableting and flow. Nemoto teaches that granules of his formulation must be useful for forming granules, have good fluidity, and be useful for the preparation of tablets with appropriate hardness.[14] Further, no evidence has been provided that decreasing granule size to that claimed would predictably provide any advantage, particularly an improved dissolution rate.

When viewing **all pertinent art** as urged in the Office Action, one would understand that decreasing granule size would reduce tableting efficiency, contrary to the teachings of Nemoto. Therefore, no reasoned explanation of a motivation to combine the references can be provided.

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9 For example, Lieberman et al. page 34, *Remington's,* 16th Edition, page 1563

10 For example, col. 2, ln. 41-63; col. 4, ln. 24-38.

11 "A claimed compound would not have been obvious where there was no reason to modify the closest prior art lead compound to the claimed compound and the prior art taught that modifying the lead compound would destroy its advantageous property" e.g., tableting, Guidelines, page 53651, col. 1-2.

12 In *DePuy Spine Inc. v. Medtronic Sofamor Danek, Inc.* (citation omitted) a rigid screw rather than a "shock absorber" screw was found to be non-obvious for use in spinal surgeries. Increasing the rigidity of the screw ran contrary to the prior art that taught increasing the rigidity of the screw would result in a greater likelihood of failure. See also *In re Hedges*, et al., 228 USPQ 685 (Fed. Cir. 1986) and *United States v. Adams*, 383 U.S. 39, 51–52, 148 USPQ 479, 483 (1966) cited in the response of 11/23/2009.

13 Guidelines, page 53647, col. 1.

14 Office Action response of 11/23/2009, pages 11-12

Third Clear Error and/or Omission in the Final Office Action:

The Examiner has made a third clear error and/or omission at least because granule size was not a results effective variable in regard to dissolution at the time of filing the application.

The Office Action has failed to provide a reference demonstrating that one of skill in the art would understand granule size to be a result-effective variable in relation to dissolution. In fact, the text cited from *Remington's*, 16th Edition (see page 1559-60) above states that the aspirin tablets having the faster dissolution rate had the slower disintegration rate. This suggests that one of skill in the art would not expect that granule size was not a result effective variable for dissolution. Remington's teaches that granule size is selected based on tablet size.[2]

In the absence of some demonstration that granule size would be considered to be a result-effective variable in relation to dissolution, the rejection must fail.[15] In the instantly claimed invention, the parameter optimized was not recognized to be a result-effective variable. Therefore, the invention cannot be obvious.

In view of the above remarks, the pending application is in condition for allowance.

Dated: November 16, 2010

Respectfully submitted,

Electronic signature: Nicholas J. DiCeglie, Jr./
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[15] *In re Antonie* (195 USPQ 6 (C.C.P.A. 1977) 195 USPQ 6) the court noted that:

In re Aller, [citation omitted], the court set out the rule that the discovery of an optimum value of a variable in a known process is normally obvious. We have found exceptions to this rule in cases where the results of optimizing a variable, which was known to be result effective, were unexpectedly good. *In re Waymouth*, [citation omitted]; *In re Saether*, supra. **This case, in which the parameter optimized was not recognized to be a result-effective variable, is another exception**. The decision of the board is reversed. (at 8-9, emphasis added)